REMARKS

Claims 1-3 and 5-63 are pending in the application. Applicants request entry and consideration of the amendments and response herein.

Amendment of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action, and was done to expedite prosecution of the application. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject mattered. Support for these amendments appears throughout the specification and claims as filed. No new matter is introduced by these amendments.

Claim Objections

Claims 5-63 are objected to as being in improper multiple dependent form. Applicants have amended claims 5-63 to proper form and request withdrawal of this objection.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-3 are rejected as failing to comply with the enablement requirement. Claim 1 is rejected in regard to step (1). In the Action, it is alleged that one of ordinary skill in the art would not know how to choose a practical set of starting materials from millions of choices, to subsequently obtain products having all desired properties. Applicants traverse.

The processes of the present application relate to selecting starting materials and reacting them in all possible combinations. The resulting scaffolds are then compared

to one another by specific criteria defined by one of ordinary skill in the art, and one or more of these scaffolds is selected for further consideration in the process. Those starting materials leading to those scaffolds are then altered and subjected to the next iteration of combination, then comparison for the specific criteria (e.g., biological activity, physicochemical parameter, etc.), leading to new compounds. The reliance in the Action on Nienaber et al. to imply that improved scaffolds, and ultimately lead compounds, cannot be efficiently arrived at using Applicants' methods without meeting, *a priori*, overarching criteria regarding desired properties in the final product, is misguided. Such a position insufficiently considers Applicants' entire process, which utilizes creation of scaffolds from combinations of starting materials, analysis of the products, and manipulation of the starting materials to provide desirable scaffolds with successive iterations. In consideration of the entire process, Applicants' methodology, in fact, does provide the Nienaber goal of identifying a "proper lead compound" in that it ultimately allows a skill artisan to inherently select increasingly suitable lead scaffolds and compounds. As stated at page 27 of the specification, "[t]the probability of discovering a product having desired properties can be estimated after 2 to 6 cycles." Such a combination of relatively minimal cycles and parallel synthesis techniques, in fact, allow for examining a large amount of chemical space without having to synthesize all possible combinations, thus increasing efficiency of the drug discovery process.

As stated on pages 12-13 of the specification, suitable representative functional groups are identified for starting materials, and in fact, diversity in the selection of functional groups provides a greater degree of chemical space representation in arriving at new compounds. One of ordinary skill in the art can select such compounds based on their inherent knowledge as well as the teachings of Applicants' specification. Once the first iteration of analysis is completed, one of skill in the art makes further guided choices with each successive iteration. Applicants submit that the processes as claimed are well within the scope of one of ordinary skill in the art (with attendant knowledge in the art) in

consideration of Applicants' specification, and that such specification is enabling to said artisan. Thus, Applicants respectfully request withdrawal of the rejection.

Claim 1 is rejected in regard to step (6) as non-enabling with regard to variants. Applicants traverse. Applicants' specification, including at pages 9, 23-24 and in the representative examples, provide description and exemplification of variants. One of ordinary skill in the art, having requisite knowledge and experience in medicinal chemistry, would be provided with guidance into selecting a variant based on a variety of factors including: (i) knowledge of the field; (ii) knowledge of the results of analysis of the first scaffold combinations (i.e., starting materials that lead to desired scaffolds); and (iii) Applicants' description and examples. As such, Applicants submit that their specification is enabling to one of ordinary skill and request that this rejection be withdrawn.

Claim 1 is rejected in regard to steps (3) and (4) as non-enabling with regard to analysis and evaluation. Applicants traverse. Pages 8-10 and 19 of Applicants' specification delineates various ways in which the analysis and evaluation can be carried out. Such evaluation can include target function, specific biological activity, and/or a spectrum of other desired pharmacological and physicochemical properties, including therapeutic properties. See, Specification at page 10. The representative examples in Applicants' specification exemplify evaluation based on biological activity (e.g., activity against Pseudomonas aeruginosa and Staphylococcus aureus) of combinatorial scaffold products as used for determination of further iterations for compound synthesis. Applicants submit that their specification in combination with the knowledge of one of ordinary skill in the art provide enabling support for their claimed subject matter and request that this rejection be withdrawn.

It is further alleged in that Action that claim 1 encompasses *in silico* methods, which one of ordinary skill would not know how to execute. Applicants traverse. Applicants submit that *in silico* methods are, in fact, within the scope of one of ordinary skill in the art. Various computational methods can be utilized to analyze potential binding,

structure conformation, lipophilicity, or other biological, pharmacological, or physicochemical properties. *In silico* methods such as those described in K. Gubernator, et al. (Eds). "Structure -Based Ligand Design", Wiley (1998) ISBN: 3-527-29343-4, are known in the art and can be used in the methods delineated herein as part of the analysis and evaluation process. As such, Applicants submit that their disclosure is enabling for *in silico* evaluative methods and request that this rejection be withdrawn.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1-3 are rejected as indefinite. Applicants traverse. Claim 1 is rejected as allegedly indefinite based on the terms "fast" and "efficient" in the preamble. Applicants have amended the claim to remove reference to such terms thus rendering the rejection moot.

Claim 1, step (8) is alleged to be inconsistent with the preamble goal. Applicants traverse. In the Action, it is alleged that the requirement of step (8) is inconsistent with the preamble goal as the goal may be achieved in step (3), and thus it is unclear why step (8) is necessary. Applicants submit that the recitation of step (8) is not inconsistent with the goal. As recited, repetition of steps (4) to (7) occurs such that "until at least one product having the desired property or properties is found." It is further alleged that step (8) allows for termination with out requiring that the product be new. Applicants have amended claim 1, step (8) to reflect the "new" product in the termination step. Based on the forgoing, Applicants submit the claim as pending is clear and not indefinite.

Claim 1 is rejected in regard to steps (3) and (4) as indefinite with regard to analysis and evaluation. Applicants traverse. Applicants have amended claim 1, steps (3) and (4) to recite "one or more biological, pharmacological, or physicochemical criterion",

thus delineating what the products are being analyzed for. Moreover, Applicants traverse the allegation in the Action that steps (3) and (4) are indefinite as it is unclear what "analysis" and "evaluation" are. As delineated in the specification, analysis refers to biological, pharmacological, or physicochemical measurement (see pages 18-19), while the evaluation (see pages 21-22) refers to more interpretive aspects including, for example, sorting, ranking, dividing or grouping the products. Applicants submit that, in light of Applicants' specification, steps (3) and (4) are indefinite to one of ordinary skill in the art and request that this rejection be withdrawn.

Claim 1, step (6) is alleged to be indefinite for the term "variant". Applicants traverse for the same reasons as delineated above. For the foregoing reasons, Applicants submit that the specification provides guidance as to variants by both description and examples, and as such, Applicants' claims are not indefinite.

Claim 1, step (7) is alleged to be indefinite as unclear as to the criteria to be used for making a determination of whether performing the reaction would be appropriate. Applicants traverse. Applicants have amended step (7) to reflect that the starting materials of step (6) are reacted with the starting materials of step (5) or "variants thereof", which includes one scenario being addressed by the "if appropriate" language (i.e., where all identified starting materials in step (5) are replaced with a variant in the next iteration). Applicants submit that the claim as amended is no longer indefinite and request withdrawal of this rejection.

Claim 1, step (8) is alleged to be indefinite as unclear as to when the desired property is determined. Applicants traverse. As delineated above, Applicants have amended claim 1 to recite "one or more physicochemical criterion", thus reciting the test and desired property. Applicants submit that the claim as amended is no longer indefinite and request withdrawal of this rejection.

Claim 1, step (9) is alleged to be indefinite as unclear as to what types of characterisation is required. Applicants traverse. Applicants have amended claim 1 to recite "physicochemical characterization" (e.g., NMR, mass spectrometry), which is delineated throughout the application as filed, including at page 28 and in the examples. Applicants submit that the claim as amended is no longer indefinite and request withdrawal of this rejection.

Claim 3 is rejected as indefinite as to the types of reactions encompassed by the process. Applicants traverse. The claim recites "MCR" reactions and the specification delineates the scope of MCR reactions at pages 12, 15, and 16. Applicants submit that the specification provides guidance as to MCR reactions by both description (including March, "*Advanced Organic Chemistry*" as cited) and examples (e.g., Passerini, Ugi, etc.) and as such, Applicants' claims are not indefinite. Applicants request withdrawal of this rejection.

In view of the above amendment, applicant believes the pending application is in condition for allowance. The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 41925-56268.

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Respectfully submitted,

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